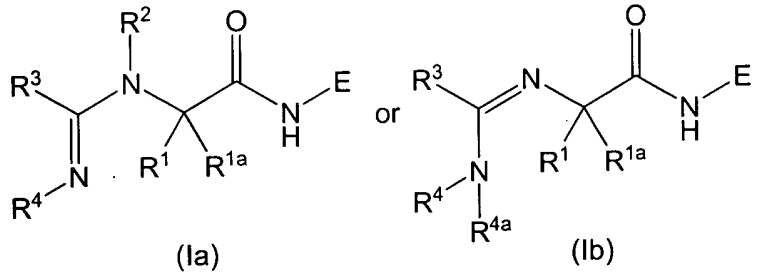
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Original) A compound of Formula (Ia) or (Ib):



wherein:

E is:

(i) $-C(R^5)(R^6)X^1$ where X^1 is -CHO, $-C(R^7)(R^8)CF_3$, $-C(R^7)(R^8)CF_2CF_2R^9$, $-C(R^7)(R^8)R^{10}$, $-CH{=}CHS(O)_2R^{10}$, $-C(R^7)(R^8)C(R^7)(R^8)OR^{10}$, $-C(R^7)(R^8)CH_2OR^{10}$, $-C(R^7)(R^8)C(R^7)(R^8)R^{10}$, $-C(R^7)(R^8)CH_2N(R^{11})SO_2R^{10}$, $-C(R^7)(R^8)CF_2C(O)NR^{10}R^{11}$, $-C(R^7)(R^8)C(O)NR^{10}R^{11}$, $-C(R^7)(R^8)C(O)N(R^{11})(CH_2)_2OR^{11}$, or $-C(R^7)(R^8)C(O)N(R^{11})(CH_2)_2NHR^{11}$;

where:

R^5 is hydrogen or (C_{1-6})alkyl;

R^6 is hydrogen, (C_{1-6})alkyl, cyano, $-X^2NR^{12}R^{12a}$, $-X^2NR^{12}C(O)R^{12a}$, $-X^2NR^{12}C(O)OR^{12a}$, $-X^2NR^{12}C(O)NR^{12a}R^{12b}$, $-X^2NR^{12}C(N^{12a})NR^{12b}R^{12C}$, $-X^2OR^{13}$, $-X^2SR^{13}$, $X^2C(O)OR^{12}$, $-X^2C(O)R^{13}$, $-X^2OC(O)R^{13}$, $-X^2C(O)NR^{12}R^{12a}$, $-X^2S(O)_2NR^{12}R^{12a}$, $-X^2NR^{12}S(O)_2R^{13}$, $-X^2P(O)(OR^{12})OR^{12a}$, $-X^2OP(O)(OR^{12})OR^{12a}$, $-X^2S(O)R^{14}$, $-X^2S(O)_2R^{14}$, R^{15}, $-X^2OR^{15}$, $-X^2SR^{15}$, $-X^2S(O)R^{15}$, $-X^2S(O)_2R^{15}$, $-X^2C(O)R^{15}$, $-X^2C(O)OR^{15}$, $-X^2OC(O)R^{15}$, $-X^2NR^{15}R^{12}$, $-X^2NR^{12}C(O)R^{15}$, $-X^2NR^{12}C(O)OR^{15}$, $-X^2C(O)NR^{15}R^{12}$, $-X^2S(O)_2NR^{15}R^{12}$,

$X^2NR^{12}S(O)_2R^{15}$, $-X^2NR^{12}C(O)NR^{15}R^{12a}$ or $-X^2NR^{12}C(NR^{12a})NR^{15}R^{12}$ where X^2 is (C_{1-6})alkylene; R^{12}, R^{12a}, R^{12b} and R^{12c} at each occurrence independently is hydrogen or (C_{1-6})alkyl; R^{13} is hydrogen, (C_{1-6})alkyl or halo-substituted$(C_{1-6}$alkyl, R^{14} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; and R^{15} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6}) alkyl, (C_{9-12})bicycloaryl(C_{0-6}) alkyl or hetero(C_{8-12})bicycloaryl(C_{0-6}) alkyl; or

R^5 and R^6 taken together with the carbon atom to which both R^5 and R^6 are attached form (C_{3-8})cycloalkylene or hetero(C_{3-8})cycloalkylene wherein said cycloalkylene and heterocycloalkylene may be substituted further with 1 to 2 radicals independently selected from (C_{1-6}) alkyl, cyano, halo, halo-substituted(C_{1-4}) alkyl, nitro, $-X^3NR^{16}R^{16a}$, $X^3N^{16}C(O)R^{16a}$, $-X^3NR^{16}C(O)OR^{16a}$, $-X^3NR^{16}C(O)NR^{16a}R^{16b}$, $-X^3NR^{16}C(NR^{16a})NR^{16b}R^{16c}$, X^3OR^{17}, $-X^3SR^{17}$, $-X^3C(O)OR^{16}$, $-X^3C(O)R^{17}$, $-X^3OC(O)R^{17}$, $-X^3C(O)NR^{16}R^{16a}$, $X^3S(O)_2NR^{16}R^{16a}$, $-X^3NR^{16}S(O)_2R^{17}$, $-X^3P(O)(OR^{16})OR^{16a}$, $-X^3OP(O)(OR^{16})OR^{16a}$, $X^3S(O)R^{18}$ and $-X^3S(O)_2R^{18}$ where X^3 is a bond or (C_{1-6}) alkylene; R^{16}, R^{16a}, R^{16b}, and R^{16c} at each occurrence independently is hydrogen or (C_{1-6})alkyl; R^{17} is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl, and R^{18} is (C_{1-6}) alkyl or halo-substituted(C_{1-6})alkyl;

R^7 is hydrogen or (C_{1-4})alkyl;

R^8 is hydroxy; or

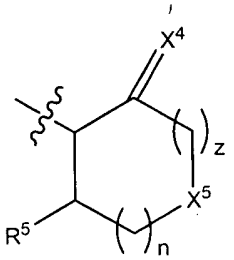
R^7 and R^8 together form oxo;

R^9 is hydrogen, halo, (C_{1-4})alkyl, (C_{5-10})aryl(C_{0-6})alkyl or hetero(C_{5-10})aryl(C_{0-6}) alkyl; and

R^{10} is (C_{1-4})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{4-10})aryl(C_{0-6})alkyl, (C_{4-10})cycloalkyl(C_{0-6})alkyl or hetero(C_{4-10})cycloalkyl(C_{0-6})alkyl; and

R^{11} is hydrogen or (C_{1-6})alkyl; or

(ii) a group of formula (a):



(a)

(a)

where:

n is 0, 1, or 2;

z is 0 or 1;

X^4 is selected from NR^{19}, S, or 0 where R^{19} is hydrogen or (C_{1-6})alkyl; and

X^5 is -O-, -S-, $-SO_2-$, or $-NR^{20}-$ where R^{20} is selected from hydrogen, (C_{1-6})alkyl, $X^6C(O)OR^{22}$, $-X^6C(O)NR^{22}R^{22a}$, $-X^6S(O)_2NR^{22}R^{22a}$, $-X^6C(O)R^{23}$, $-X^6S(O)_2R^{24}$, $-R^{25}$, $-X^6C(O)OR^{25}$, $-X^6C(O)NR^{22}R^{25}$, $-X^6S(O)_2NR^{22}R^{25}$, $-X^6C(O)R^{25}$ and $-X^6S(O)_2R^{25}$ in which X^6 is a bond or (C_{1-6})alkylene; R^{22} and R^{22a} at each occurrence independently is hydrogen or (C_{1-6})alkyl; R^{23} is hydrogen, (C_{1-6}) alkyl or halo-substituted(C_{1-6})alkyl, R^{24} is (C_{1-6})alkyl or halo-substituted(C_{1-6}) alkyl, and R^{25} is (C_{3-10})cycloalkyl(C_{0-6}) alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-12})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-6})alkyl provided that when R^5 is hydrogen, then both X^4 and X^5 are not -0-;

R^5 is as defined above;

and furthermore within E any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with R^x selected from $-R^{26}$, $-X^7OR^{26}$, $-X^7SR^{26}$, $-X^7S(O)R^{26}$, $-X^7S(O)_2R^{26}$, $-X^7C(O)R^{26}$, $-x^7C(O)OR^{26}$, $-X^7OC(O)R^{26}$, $-X^7NR^{26}R^{27}$, $-X^7NR^{27}C(O)R^{26}$, $-X^7NR^{27}C(O)OR^{26}$, $X^7C(O)NR^{26}R^{27}$, $-X^7S(O)_2NR^{26}R^{27}$, $-X^7NR^{27}S(O)_2R^{26}$, $-X^7NR^{27}C(O)NR^{26}R^{27a}$ and

$-X^7NR^{27}C(NR^{27a})NR^{26}R^{27b}$ and wherein E and R^x may be substituted further with 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^8NR^{28}R^{28a}$, $-X^8NR^{28}C(O)R^{28a}$, $-X^8NR^{28}C(O)OR^{28a}$, $-X^8NR^{28}C(O)NR^{28a}R^{28b}$, $X^8NR^{28}C(NR^{28a})NR^{28b}R^{28c}$, $-X^80R^{29}$, $-X^8SR^{29}$, $-X^8C(0)0R^{28}$, $-X^8C(O)R^{29}$, $-X^8OC(O)R^{29}$, $-X^8C(O)NR^{28}R^{28a}$, $-X^8S(O)_2NR^{28}R^{28a}$, $-X^8NR^{28}S(O)_2R^{29}$, $-X^8P(O)(OR^{28})OR^{28a}$, $-X^8OP(O)(OR^{28})OR^{28a}$, $-X^8S(O)R^{30}$ and $-X^8S(O)_2R^{30}$ wherein X^7 and X^8 are independently a bond or (C_{1-6})alkylene; R^{26} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-12})bicycloaryl$(C_{0-6}$alkyl or hetero(C_{8-12})bicycloaryl(C_{0-6})alkyl, R^{27}, R^{27a}, R^{27b}, R^{28}, R^{28a}, R^{28b} and R^{28c} at each occurrence independently is hydrogen or (C_{1-6})alkyl, R^{29} is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl, and R^{30} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl;

R^1 is (C_{1-10})alkyl or $-C(R^{31})(R^{32})X^9$ wherein R^{31} and R^{32} are independently hydrogen or (C_{1-6})alkyl and X^9 is selected from $-X^{10}NR^{33}R^{33a}$, $-X^{10}NR^{33}C(O)R^{33a}$, $-X^{10}NR^{33}C(O)OR^{33a}$, $X^{10}NR^{33}C(O)NR^{33a}R^{33b}$, $-X^{10}NR^{33}C(NR^{33a})NR^{33b}R^{33c}$, $-X^{10}OR^{33}$, $-X^{10}SR^{33}$, $-X^{10}C(O)OR^{33}$, $-X^{10}C(O)R^{33}$, $-X^{10}OC(O)R^{33}$, $-X^{10}C(O)NR^{33}R^{33a}$, $-X^{10}S(O)_2NR^{33}R^{33a}$, $-X^{10}NR^{33}S(O)_2R^{33a}$, $X^{10}P(O)(OR^{33})OR^{33a}$, $-X^{10}OP(O)(OR^{33})OR^{33a}$, $-X^{10}C(O)R^{34}$, $-X^{10}NR^{33}C(O)R^{34}$, $-_X{}^{10}S(O)R^{34}$, $X^{10}S(O)_2R^{34}$, $-R^{35}$, $-X^{10}OR^{35}$, $-X^{10}SR^{35}$, $-X^{10}S(O)R^{35}$, $-X^{10}S(O)_2R^{35}$, $-X^{10}C(O)R^{35}$, $-X^{10}C(O)OR^{35}$, $-X^{10}OC(O)R^{35}$, $-X^{10}NR^{33}R^{35}$, $-X^{10}NR^{33}C(O)R^{35}$, $-X^{10}NR^{33}C(O)OR^{35}$, $-X^{10}C(O)NR^{33}R^{35}$, $-X^{10}S(O)_2NR^{33}R^{35}$, $-X^{10}NR^{33}S(O)_2R^{35}$, $-X^{10}NR^{33}C(O)NR^{33a}R^{35}$ and $-X^{10}NR^{33}C(NR^{33a})NR^{33b}R^{35}$ wherein X^{10} is a bond or (C_{1-6})alkylene; R^{33}, R^{33a}, R^{33b}, and R^{33c} at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; R^{34} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; and R^{35} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-10})bicycloaryl(C_{0-6})alkyl;

wherein within R^1 any alicyclic or aromatic ring system is unsubstituted or substituted further by 1 to 5 radicals independently selected from (C_{1-6})alkyl, (C_{1-6})alkylidene, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^{11}NR^{36}R^{36a}$, $-X^{11}NR^{36}C(O)R^{36a}$, $-X^{11}NR^{36c}(O)OR^{36a}$, $-X^{11}NR^{36}C(O)NR^{36a}R^{36b}$, $-X^{11}NR^{36}C(NR^{36a})NR^{36b}R^{36c}$, $-X^{11}OR^{36}$, $X^{11}SR^{36}$,

$-X^{11}C(O)OR^{36}$, $-X^{11}C(O)R^{36}$, $-X^{11}OC(O/)R^{36}$, $-X^{11}C(O)NR^{36}R^{36a}$, $X^{11}S(O)_2NR^{36}R^{36a}$, $-X^{11}NR^{36}S(O)_2R^{36a}$, $-X^{11}P(O)(OR^{36})OR^{36a}$, $-X^{11}OP(O)(OR^{36})OR^{36a}$, $X^{11}NR^{36}C(O)R^{37}$, $-X^{11}S(O)R^{37}$, $-X^{11}C(O)R^{37}$ and $-X^{11}S(O)_2R^{37}$ and/or 1 radical selected from $-R^{38}$, $-X^{12}0R^{38}$, $-X^{12}SR^{38}$, $-X^{12}S(O)R^{38}$, $-X^{12}S(O)_2R^{38}$, $-X^{12}C(O)R^{38,}$ $-X^{12}C(O)OR^{38}$, $X^{12}OC(O)R^{38}$, $X^{12}NR^{36}R38$, $-X^{12}NR^{36}C(O)R^{38}$, $-X^{12}NR^{36}C(O)0R^{38}$, $-X^{12}C(O)NR^{36}R^{38}$, $X^{12}S(O)_2NR^{36}R^{38}$, $-X^{12}NR^{36}S(O)_2R^{38}$, $-X^{12}NR^{36}C(O)NR^{36a}R^{38}$ and $-X^{12}NR^{36}C(N^{36a})NR^{36b}R^{38}$; and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 5 radicals independently selected from cyano, halo, nitro, $-NR^{39}R^{39a}$, $N^{39}C(O)R^{39a}$, $-NR^{39}C(O)OR^{39a}$, $-NR^{39}C(O)NR^{39a}R^{39b}$, $-NR^{39}C(NR^{39a})NR^{39b}R^{39c}$, $-OR^{39}$, $-SR^{39}$, $-C(O)OR^{39}$, $-C(O)R^{39}$, $-OC(O)R^{39}$, $-C(O)NR^{39}R^{39a}$, $-S(0)_2NR^{39}R^{39a}$, $-NR^{39}S(O)_2R^{39a}$, $-P(O)(OR^{39})OR^{39a}$, $-OP(O)(OR^{39})OR^{39a}$, $-NR^{39}C(O)R^{40}$, $-S(O)R^{40}$ and $-S(O)_2R^{40}$; wherein X^{11} and X^{12} are independently a bond or (C_{1-6})alkylene; R^{36}, R^{36a}, R^{36b}, R^{36c}, R^{39}, R^{39a}, R^{39b} and R^{39c} at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})aIkyl; R^{37} and R^{40} are independently (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; and R^{38} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{6-10})bicycloaryl(C_{0-6})alkyl, provided that only one (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-10})bicycloaryl(C_{0-6})alkyl ring structure is present within R^1;

R^{1a} is hydrogen or (C_{1-6})alkyl; or

R^1 and R^{1a} together with the carbon atoms to which they are attached form (C_{3-8})cycloalkylene or hetero(C_{3-10})cycloalkylene ring wherein said cycloalkylene ring is optionally substituted with one or two substitutents independently selected from (C_{1-6})alkyl, (C_{1-6})alkoxy, hydroxy, halo, hydroxyalkyl, or keto and said heterocycloalkylene ring is optionally substituted with one or two substitutents independently selected from (C_{1-6})alkyl, (C_{1-4})alkoxy, hydroxyalkyl, alkoxyalkyl, aminoalkyl, acyl, (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl wherein said aryl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, or three substitutents independently selected from (C_{1-4})alkyl, (C_{1-6})alkoxy, nitro, amino, halo, hydroxy,

alkylthio, halo-substituted alkyl, halo-substituted alkoxy, acyl, $-OC(O)R^{39}$, $-C(O)NR^{39}R^{39a}$, $-S(O)_2NR^{39}R^{39a}$, $-S(O)_2R^{38}$ or $-S(O)_2R^4$ where R^{38}, R^{39}, R^{39a}, and R^4 are as defined above;

R^2 is hydrogen, hydroxy, or (C_{1-6})alkyl;

R^3 is hydrogen, (C_{1-6})alkyl, (C_{1-6})alkoxy, aryloxy, (C_{3-8})cycloalkyl, (C_{3-8})cycloalkyloxy, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, (C_{1-6})alkylsulfonyl(C_{1-6})alkyl, (C_{3-8})cycloalkylsulfonyl(C_{1-6})alkyl, arylsulfonyl(C_{1-6})alkyl, heterocyclic ring selected from azepanyl, azocanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, tetrahydropyranyl, tetrahydrothiopyranyl, thiopyranyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, tetrazolyl, pyrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzisoxazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, tetrahydroquinazolinyl, benzoxazolyl or quinoxalinyl, -OR where R is a heterocyclic moiety selected from those herein described in this paragraph, or amino; wherein R^3 is optionally substituted by one, two, or three R^a;

each R^a is independently (C_{1-6})alkyl, (C_{3-8})cycloalkyl, aryl, tetrahydronaphthyl, indenyl, indanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, (C_{1-6})alkoxy, (C_{1-6})haloalkoxy, (C_{1-6})alkanoyl, (C_{1-6}) alkanoyloxy, aryloxy, benzyloxy, (C_{1-6})alkoxycarbonyl, aryloxycarbonyl, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-6})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently (C_{1-6})alkanoylamino, aroylamino, (C_{1-6})alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by (C_{1-6})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently (C_{1-6})alkoxycarbonylamino, aryloxycarbonylamino, (C_{1-6})alkylcarbamoyloxy, arylcarbamoyloxy, (C_{1-6})alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, (C_{1-6})alkylaminosulfonyl, di-(C_{1-6})alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-6})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyridinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently halogen, hydroxy, (C_{1-6})alkoxy, (C_{1-6})haloalkyl, (C_{1-6})haloalkoxy, oxo, carboxy, cyano, nitro, carboxamide, amidino or guanidino, R^a is may be further optionally substituted by one, two, or three R^b;

each R^b is independently (C_{1-6})alkyl optionally partially or fully halogenated wherein one or more carbon atoms are optionally replaced by O, N, S(O), $S(O)_2$ or S and wherein said alkyl is optionally independently substituted with 1-2 oxo groups, $-NH_2$, or one or more C_{1-4} alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl; or

each R^b is independently (C_{1-6})cycloalkyl, aryl, aryloxy, benzyloxy, halogen, hydroxy, (C_{1-6})alkyl, (C_{1-6})alkoxy, (C_{1-6})haloalkyl, (C_{1-6})haloalkoxy, aminosulfonyl,

(C_{1-6})alkylaminosulfonyl, di-(C_{1-6})alkylaminosulfonyl, arylaminosulfonyl, oxo, carboxy, cyano, nitro, mono-C_{1-5}alkylamino, di-(C_{1-5})alkylamino, carboxamide, amidino or guanidino;

R^4 is hydrogen, hydroxy, nitrile, or a (C_{1-6})alkyl optionally partially or fully halogenated wherein one or more C atoms are optionally replaced by O, NH, S(O), $S(O)_2$ or S and wherein said alkyl chain is optionally independently substituted with 1-2 oxo groups, $-NH_2$, one or more C_{1-4} alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl; or

R^3 and R^4 together with the atoms to which they are attached form a heterocycloalkyl ring or a heterocyclic ring fused to an aryl or heteroaryl ring provided that the heterocycloalkyl rings contain at least an $-SO_2-$ group, wherein said heterocycloalkyl rings may be optionally substituted on the aromatic and/or non-aromatic portion of the rings with one, two, or three R^c;

each R^c and R^{4a} is independently:

hydrogen, (C_{1-6})alkyl optionally interrupted by one or two N, O, S, S(O), or $S(O)_2$ and optionally substituted by 1-2 oxo, amino, hydroxy, halogen, C_1 alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl;

halo, alkoxy, alkylthio, hydroxy, carboxy, aryl, aryloxy, aroyl, heteroaryl, (C_{1-6})alkanoyl, $-C(O)OR^d$ where (R^d is hydrogen, (C_{1-6})alkyl, (C_{1-6})alkoxyalkyl, (C_{1-6})haloalkyl, (C_{3-7})cycloalkyl, (C_{3-7})cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl, aryl, or aryl(C_{1-6})alkyl), (C_{1-6})alkylsulfonyl, aryloxycarbonyl, benzyloxycarbonyl, (C_{1-6})alkanoylamino, aroylamino, C_{1-5} alkylthio, arylthio, (C_{1-6})alkylsulfonylamino, arylsulfonylamino,

(C_{1-6})alkylamino-sulfonyl, arylaminosulfonyl, (C_{3-6})cycloalkyl and benzyloxy wherein each of the aforementioned group is optionally substituted with halogen, hydroxy, (C_{1-6})alkyl, (C_{1-6})alkoxy, (C_{1-6})haloalkyl, (C_{1-6})haloalkoxy, oxo, carboxy, nitrile, nitro or $NH_2C(O)$-; or a pharmaceutically acceptable salts thereof provided that there are no more than 5 ring systems in a compound of Formula (Ia) or (Ib).

2. (Original) The compound of Claim 1 wherein:

R^3 is (C_{1-6})alkyl, (C_{1-6})alkoxy, aryloxy, (C_{3-8})cycloalkyl, (C_{3-8})cycloalkyloxy, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, (C_{1-6})alkylsulfonyl(C_{1-6})alkyl, (C_{3-8})cycloalkylsulfonyl(C_{1-6})alkyl, arylsulfonyl(C_{1-6})alkyl, heterocyclic ring selected from azepanyl, azocanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, tetrahydropyranyl, tetrahydrothiopyranyl, thiopyranyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, tetrazolyl, pyrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzisoxazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, tetrahydroquinazolinyl, benzoxazolyl or quinoxalinyl, -OR where R is a heterocyclic moiety selected from those herein described in this paragraph, or amino; wherein R^3 is optionally substituted by one, two, or three R^a;

each R^a is independently (C_{1-6})alkyl, (C_{3-8})cycloalkyl, aryl, tetrahydronaphthyl, indenyl, indanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, (C_{1-6})alkoxy, (C_{1-6})haloalkoxy, (C_{1-6})alkanoyl, (C_{1-6}) alkanoyloxy, aryloxy, benzyloxy, (C_{1-6})alkoxycarbonyl, aryloxycarbonyl, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-4})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or each

R^a is independently (C_{1-6})alkanoylamino, aroylamino, (C_{1-6})alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureid'o wherein either nitrogen atom may be independently substituted by (C_{1-6})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently (C_{1-6})alkoxycarbonylamino, aryloxycarbonylamino, (C_{1-6})alkylcarbamoyloxy, arylcarbamoyloxy, (C_{1-6})alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, (C_{1-6})alkylaminosulfonyl, di-(C_{1-6})alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-6})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyridinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently halogen, hydroxy, (C_{1-6})alkoxy, (C_{1-6})haloalkyl, (C_{1-6})haloalkoxy, oxo, carboxy, cyano, nitro, carboxamide, amidino or guanidino, R^a is may be further optionally substituted by one, two, or three R^b;

each R^b is independently (C_{1-6})alkyl optionally partially or fully halogenated wherein one or more carbon atoms are optionally replaced by O, N, S(O), $S(O)_2$ or S and wherein said alkyl is optionally independently substituted with 1-2 oxo groups, $-NH_2$, or one or more C_{1-4} alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl; or

each R^b is independently (C_{3-6})cycloalkyl, aryl; aryloxy, benzyloxy, halogen, hydroxy, (C_{1-6})alkyl, (C_{1-6})alkoxy, (C_{1-6})haloalkyl, (C_{1-6})haloalkoxy, aminosulfonyl,

(C_{1-6})alkylaminosulfonyl, di-(C_{1-6})alkylaminosulfonyl, arylaminosulfonyl, oxo, carboxy, cyano, nitro, mono-C_{1-5})alkylamino, di-(C_{1-5})alkylamino, carboxamide, amidino or guanidino; or

R^3 and R^4 in (Ia) or (Ib) together with the atoms to which they are attached form a heterocycloalkyl ring or a heterocycloalkyl ring fused to an aryl or heteroaryl ring provided the heterocyclic rings contain at least an -SO_2- group, wherein said heterocycloalkyl rings are optionally substituted on the aromatic and/or non-aromatic portion of the rings with one, two, or three R^c;

each R^c and R^{4a} is hydrogen, (C_{1-6})aIkyl optionally interrupted by one or two N, O, S, S(O), or $S(O)_2$ and optionally substituted by 1-2 oxo, amino, hydroxy, halogen, C_{1-6})alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indoly], benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl;

halo, alkoxy, alkylthio, hydroxy, carboxy, aryl, aryloxy, aroyl, furanyl, thienyl, pyrrolyl, imidazolyl, pyridinyl, pyrimidinyl, (C_{1-6})alkanoyl, -C(O)OR^d where (R^d is hydrogen, (C_{1-6})alkyl, (C_{1-6})alkoxyalkyl, (C_{1-6})haloalkyl, (C_{3-7})-cycloalkyl, (C_{3-7})-cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-4})alkyl, aryl, or aryl(C_{1-6})alkyl), (C_{1-6})-alkylsulfonyl, aryloxycarbonyl, benzyloxycarbonyl, (C_{1-6})alkanoylamino, aroylamino, C_{1-5} alkylthio, arylthio, (C_{1-6})alkylsulfonylamino, arylsulfonylamino, (C_{1-6})alkylamino-sulfonyl, arylaminosulfonyl, (C_{3-6})cycloalkyl and benzyloxy wherein each of the aforementioned group is optionally substituted with halogen, hydroxy, (C_{1-6})alkyl, (C_{1-6})alkoxy, (C_{1-6})-haloalkyl, (C_{1-6})haloalkoxy, oxo, carboxy, nitrile, nitro, or $NH_2C(O)$-.

3. (Original) The compound of Claim 2 wherein E is -$CHR^6C(O)R^{10}$ where R^6 is saturated alkyl, and R^{10} is hetero(C_{4-10})aryl optionally substituted with (C_{3-10})cycloalkyl, (C_{6-10})aryl [optionally substituted with -$NR^{28}R^{28a}$, -OR^{29}, or halo substituted (C_{1-4}) saturated alkyl], hetero(C_{5-10})aryl, (C_{1-6}) saturated alkyl, halo-substituted (C_{1-4}) saturated alkyl, or -X^8OR^{29}

where X^8 is (C_{1-6}) saturated alkylene, R^{28} and ^{R28a} are independently hydrogen or (C_{1-6}) saturated alkyl, R^{29} is hydrogen, (C_{1-6}) saturated alkyl, or halo-substituted (C_{1-6}) saturated alkyl.

4. (Original) The compound of Claim 3 wherein R^1 is $-CH_2X^9$ wherein X^9 is selected from $-X^{10}SR^{33}$, $-X^{10}C(O)NR^{33}R^{33a}$, $-X^{10}S(O)_2R^{34}$, $-X^{10}COR^{34}$, $-X^{10}OR^{33}$, $-R^{35}$, $-X^{10}SR^{35}$, $-X^{10}S(O)2R^{35}$, $-X^{10}C(O)R^{35}$, or $-X^{10}C(O)NR^{33}R^{35}$ wherein X^{10} is a bond or (C_{1-6})alkylene; R^{33} and R^{33a} at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; R^{34} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; and R^{35} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl$(C_{0-6}$alkyl, hetero(C_{5-10})aryl$(C_{0-6}$alkyl, (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-10})bicycloaryl(C_{0-6})-alkyl wherein within R^1 any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C_{1-6}) saturated alkyl, benzyl, cyano, halo, halo-substituted(C_{1-4}) saturated alkyl, $-OR^{36}$, or $-R^{38}$ where R^{36} is (C_{1-6}) saturated alkyl or halo-substituted(C_{1-6}) saturated alkyl and R^{38} is (C_{6-10})aryl and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo; and R^{1a} is hydrogen.

5. (Original) The compound of Claim 3 wherein R^1 is 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, tert-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonylmethyl, pyridin-4-ylmethanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethanesulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloropropyl, 2,2-dichloro-3-phenylpropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothien-2-ylmethyl, pyridin-4-ylmethyl, 2,2-dichloroethyl, 2,2,2-trichloroethyl, 1,4-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, isopropylmethanesulfonylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl and ^{1a} is hydrogen.

6. (Original) The compound of Claim 4 wherein R^3 is (C_{1-5})alkyl, (C_{3-6})cycloalkyl, phenyl, benzyl, naphthyl, (C_{1-3})alkylsulfonyl(C_{1-3})alkyl, (C_{3-6})cycloalkylsulfonyl(C_{1-3})alkyl, arylsulfonyl(C_{1-3})alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, isoxazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, quinolinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl or amino; wherein R^3 is optionally substituted by one, two, or three substituents independently selected from R^a;

each R^a is independently (C_{1-3})alkyl, cyclopropyl, cyclopentyl, cyclohexyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, (C_{1-3})alkoxy, (C_{1-3})alkanoyl, (C_{1-3})alkanoyloxy, aryloxy, benzyloxy, (C_{1-3})alkoxycarbonyl, aryloxycarbonyl, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-3})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, benzimidazolyl or benzthiazolyl, or

each R^a is independently (C_{1-3})alkanoylamino, aroylamino, (C_{1-3})alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by (C_{1-3})alkyl, aryl, pyrrolidinyl, piperidinyl,morpholinyl, thiomorpholinyl or piperazinyl, or

each R^a is independently (C_{1-3})alkoxycarbonylamino, aryloxycarbonylamino, (C_{1-3})alkylcarbamoyloxy, arylcarbamoyloxy, (C_{1-3})alkylsulfonylamino, arylsulfonylamino, (C_{1-3})alkylamino-sulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-3})alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl or piperazinyl, or

each R^a is independently halogen, hydroxy, oxo, carboxy, cyano, nitro, carboxamide, amidino, or guanidino, R^a may be further optionally substituted by one, two or

three R^b; each R^b is independently (C_{1-3})alkyl, aryl, (C_{1-3})alkoxy, (C_{1-3})haloalkyl, (C_{1-3})haloalkoxy, aryloxy, benzyloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, carboxamide, amidino or guanidino;

R^2 and R^4 are hydrogen; and

R^{4a} is $-C(O)OR^d$ where (R^d is hydrogen, (C_{1-6})alkyl, (C_{1-6})alkoxy(C_{1-6})alkyl, (C_{1-6})haloalkyl, (C_{3-7})cycloalkyl, (C_{3-7})cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-6})alkyl, awl, or aryl(C_{1-6})alkyl).

7. (Original) The compound of Claim 4 wherein R^2 and R^{4a} are hydrogen;

R^3 is (C_{1-6}) saturated alkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, pyridinyl, or amino; wherein R^3 is optionally substituted by one, two or three R^a where each R^a is independently halo or (C_{1-6}) saturated alkyl; and

R^4 is hydrogen, (C_{1-6}) saturated alkyl, or halogenated alkyl.

8. (Original) The compound of Claim 4 wherein R^2 and R^{4a} are hydrogen and R^3 and R^4 together with the atoms to which they are attached form a 5 or 6 membered heterocycloalkyl ring containing at least an $-SO_2-$ group or a 5 or 6 membered heterocycloalkyl ring containing at least an $-SO_2-$ group and is fused to a phenyl, thienyl, pyrrolyl, or pyridinyl ring optionally independently substituted by one or two R^c.

9. (Original) The compound of Claim 1 wherein:

R^{la}, R^2, R^3 and R^{4a} are hydrogen;

R^1 is $-CH_2X^9$ wherein X^9 is selected from $-X^{10}SR^{33}$, $-X^{10}C(O)NR^{33}R^{33a}$, $-X^{10}S(O)_2R^{34}$, $-X^{10}COR^{34}$, $-X^{10}OR^{33}$, $-R^{35}$, $-X^{10}SR^{35}$, $-X^{10}S(O)^2R^{35}$, $-X^{10}C(O)R^{35}$, or $X^{10}C(O)NR^{33}R^{35}$ wherein X^{10} is a bond or (C_{1-6})alkylene; R^{33} and ^{R33a} at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; R^{34} is (C_{1-6})alkyl or halo-

substituted(C_{1-6})alkyl; and R^{35} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-10})bicycloaryl(C_{0-6})-alkyl wherein within R^1 any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C_{1-6}) saturated alkyl, benzyl, cyano, halo, halo-substituted(C_{1-6}) saturated alkyl, -OR^{36}, or -R^{38} where R^{36} is (C_{1-6}) saturated alkyl or halo-substituted(C_{1-6}) saturated alkyl and R^{38} is (C_{6-10})aryl and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo;

E is -$CHR^6C(O)R^{10}$ where R^6 is saturated alkyl, and R^{10} is hetero(C_{4-10})aryl optionally substituted with (C_{3-10})cycloalkyl, (C_{6-10})aryl [optionally substituted with -$NR^{28}R^{28a}$, -OR^{29}, or halo substituted (C_{1-4}) saturated alkyl], hetero(C_{5-10})aryl, (C_{1-6}) saturated alkyl, halo-substituted (C_1**4** saturated alkyl, or -X^8OR^{29} where X^8 is (C_{1-6}) saturated alkylene, R^{28} and R^{28a} are independently hydrogen or (C_{1-6}) saturated alkyl, R^{29} is hydrogen, (C_{1-6}) saturated alkyl, or halo-substituted (C_{1-6}) saturated alkyl; and

R^4 is -SO_2R where R is pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl, or quinoxalinyl, -SO_2-saturated alkyl, (C_{1-6}) saturated alkyl substituted with a heteroaryl ring defined immediately above or pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, or indolinyl, -SO_2NRR' where R and R' are independently hydrogen or (C_{1-6}) saturated alkyl wherein each of the aforementioned group is optionally substituted with halogen, hydroxy, (C_{1-6}) saturated alkyl, (C_{1-6}) saturated alkoxy, (C_{1-6}) saturated haloalkyl, (C_{1-6}) saturated haloalkoxy, oxo, carboxy, nitrile, nitro or -$CONH_2$-.

10. (Original) The compound of Claim 1 wherein:

R^{1a}, R^2 and R^4 are hydrogen;

R^1 is -CH_2X^9 wherein X^9 is selected from -$X^{10}SR^{33}$, -$X^{10}C(O)NR^{33}R^{33a}$ -$X^{10}S(O)_2R^{34}$, -$X^{10}COR^{34}$, -$x^{10}OR^{33}$, -R^{35}, -$X^{10}SR^{35}$, -$X^{10}S(O)^2R^{35}$, -$x^{10}C(O)R^{35}$, or

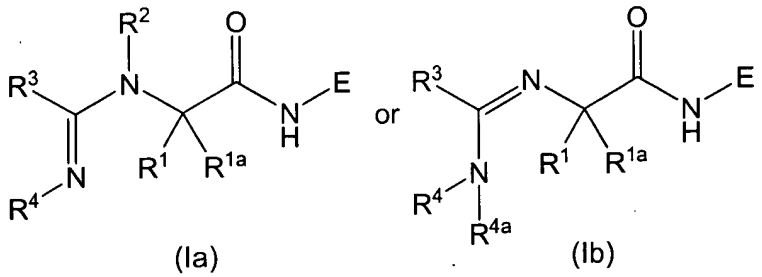
$-X^{10}C(O)NR^{33}R^{35}$ wherein X^{10} is a bond or (C_{1-6})alkylene; R^{33} and ^{R33a} at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; R^{34} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; and R^{35} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-10})bicycloaryl(C_{0-6})-alkyl wherein within R^1 any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C_{1-6}) saturated alkyl, benzyl, cyano, halo, halo-substituted(C_{1-4}) saturated alkyl, $-OR^{36}$, or $-R^{38}$ where R^{36} is (C_{1-6}) saturated alkyl or halo-substituted(C_{1-6}) saturated alkyl and R^{38} is (C_{1-6})aryl and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo;

E is $-CHR^6C(O)R^{10}$ where R^6 is saturated alkyl, and R^{10} is hetero(C_{4-10})aryl optionally substituted with (C_{3-10})cycloalkyl, (C_{6-10})aryl [optionally substituted with $-NR^{28}R^{28a}$, $-OR^{29}$, or halo substituted (C_{1-4}) saturated alkyl], hetero(C_{5-10})aryl, (C_{1-6}) saturated alkyl, halo-substituted (C_{1-4}) saturated alkyl, or $-X^8OR^{29}$ where X^8 is (C_{1-6}) saturated alkylene, R^{28} and R^{28a} are independently hydrogen or (C_{1-6}) saturated alkyl, R^{29} is hydrogen, (C_{1-6}) saturated alkyl, or halo-substituted (C_{1-6}) saturated alkyl;

R^3 is hydrogen, (C_{1-6}) saturated alkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, pyridinyl, or amino; wherein R^3 is optionally substituted by one, two or three R^a where R^a is halo or (C_{16}) saturated alkyl; and

R^{4a} is heteroaryl, (C_{1-6}) saturated alkylsulfonyl, or (C_{1-6}) halo-substituted saturated alkylsulfonyl.

11. (Original) A compound of Formula (Ia) or (Ib):



(Ia) or (Ib)

wherein:

R^{1a}, R^2 and R^{4a} are hydrogen;

E is $-CHR^6C(O)R^{10}$ where R^6 is ethyl, propyl, or butyl, and R^{10} is hetero(C_{4-10})aryl optionally substituted with (C_{3-10})aryl, (C_{6-10})aryl, hetero(C_{5-10})aryl, (C_{1-6})alkyl, halo, halo-substituted (C_{1-4})alkyl, $NR^{28}R^{28a}$, $-OR^{29}$, or $-COOR^{28}$, $-COR^{29}$ where R^{28} and R^{28a} are independently hydrogen or -(C_{1-6})alkyl, R^{29} is hydrogen, -(C^{1-6})alkyl, or halo-substituted -(C_{1-6})alkyl;

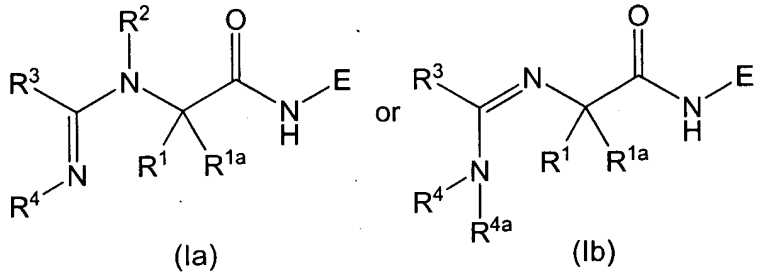
R^1 is 2,2-dichloroethyl, 2,2,2-trichloroethyl, isopropylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, *tert*-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonyl-methyl, pyridin-4-yl-methanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethane-sulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-dichloropropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothien-2-ylmethyl, pyridin-4-ylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl;

R^3 is hydrogen, (C_{1-6}) saturated alkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, pyridinyl, or amino; wherein R^3 is

optionally substituted by one, two or three R^a where each R^a is independently halo or (C_{1-6}) saturated alkyl; and

R^4 is hydrogen, (C_{1-6}) saturated alkyl, halo-substituted saturated alkyl, or (C_{1-6}) saturated alkylsulfonyl.

12. (Original) A compound of Formula (Ia) or (Ib):



wherein:

R^{1a}, R^2 and R^{4a} are hydrogen;

E is $-CHR^6C(O)R^{10}$ where R^6 ethyl and R^{10} is benzoxazol-2-yl, oxazolo[4,5-b]pyridin-2-yl, 2-pyridin-3-yl-[1,3,4]-oxadiazol-5-yl, 2-pyridin-4-yl- [1,3,4]-oxadiazol-5-yl, 2-ethyl-[1,3,4]-oxadiazol-5-yl, 2-isopropyl-[1,3,4]-oxadiazol-5-yl, 2-*tert*-butyl-[1,3,4]-oxadiazol-5-yl, 2-phenyl-[1,3,4]-oxadiazol-5-yl, 2-methoxymethyl-[1,3,4]-oxadiazol-5-yl, 2-furan-2-yl-[1,3,4]-oxadiazol-5-yl, 2-thien-2-yl-[1,3,4]-oxadiazol-5-yl, 2-(4-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-dimethylaminophenyl)-[1,3,4]-oxadiazol-5-yl, pyradizin-3-yl, pyrimidin-2-yl, 3-phenyl-[1,2,4]-oxadiazol-5-yl, 3-ethyl-[1,2,4]-oxadiazol-5-yl, 3-cyclopropyl-[1,2,4]-oxadiazol-5-yl, 3-thien-3-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-4-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-2-yl-[1,2,4]-oxadiazol-5-yl, 5-ethyl-[1,2,4]-oxadiazol-3-yl, 5-phenyl-[1,2,4]-oxadiazol-3-yl, 5-thien-3-yl-[1,2,4]-oxadiazol-3-yl, 5 -trifluoromethyl- [1,2,4]-oxadiazol-3-yl, 5-pyridin-4-yl-[1,2,4]-oxadiazol-3-yl, or 5-phenyloxazol-2-yl;

2,2-dichloroethyl, 2,2,2-trichloroethyl, isopropylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, *tert*-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonyl-methyl, pyridin-4-yl-methanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethane-sulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-dichloropropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothien-2-ylmethyl, pyridin-4-ylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl;

R^3 is methyl, trifluoromethyl, 2,2,2-trifluoroethylamino, amino, *N,N*-dimethylamino, morpholin-4-yl, pyrrolidin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-5-yl, pyrimidin-4-yl, oxazol-4-yl, oxazol-5-yl, thiazol-4-yl, thiazol-5-yl, quinolin-6-yl, indol-5-yl, 2-methylimidazol-4-yl, phenyl, or 4-fluorophenyl; and

R^4 is hydrogen, 2,2,2-trifluoroethyl, methyl, or methylsulfonyl.

13. (Original) The compound of Claim 11 wherein R^4 is 2,2,2-trifluoroethyl.

14. (Original) The compound of Claim 12 wherein R^4 is 2,2,2-trifluoroethyl.

15. (Original) The compound of Claim 1 wherein:

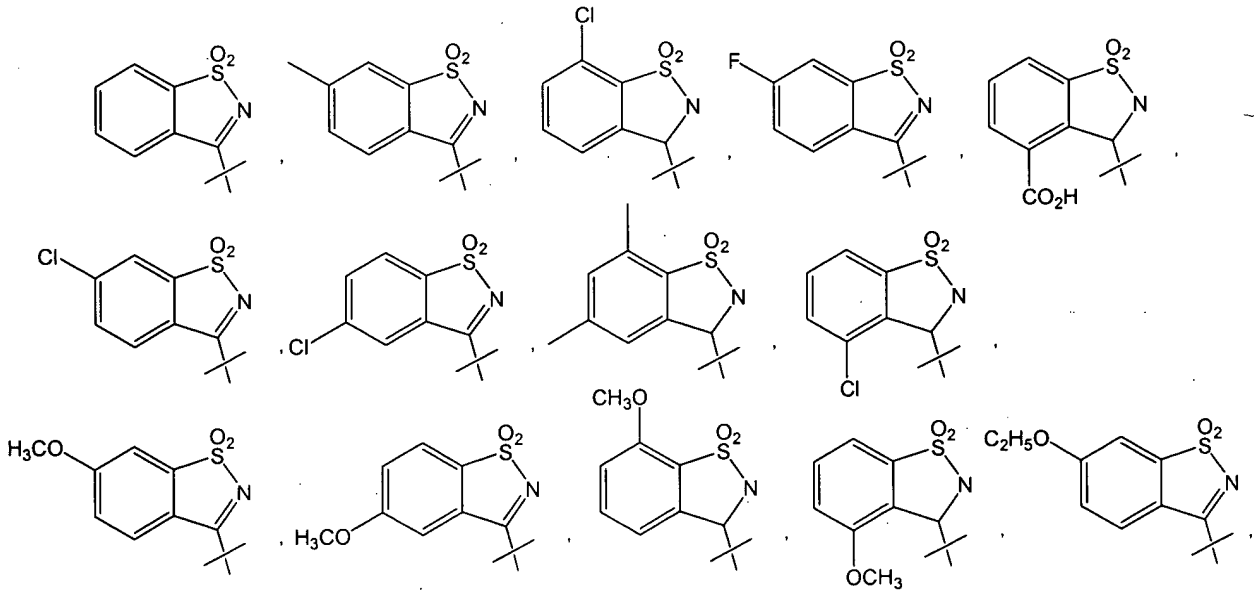
R^{1a}, R^2 and R^{4a} are hydrogen;

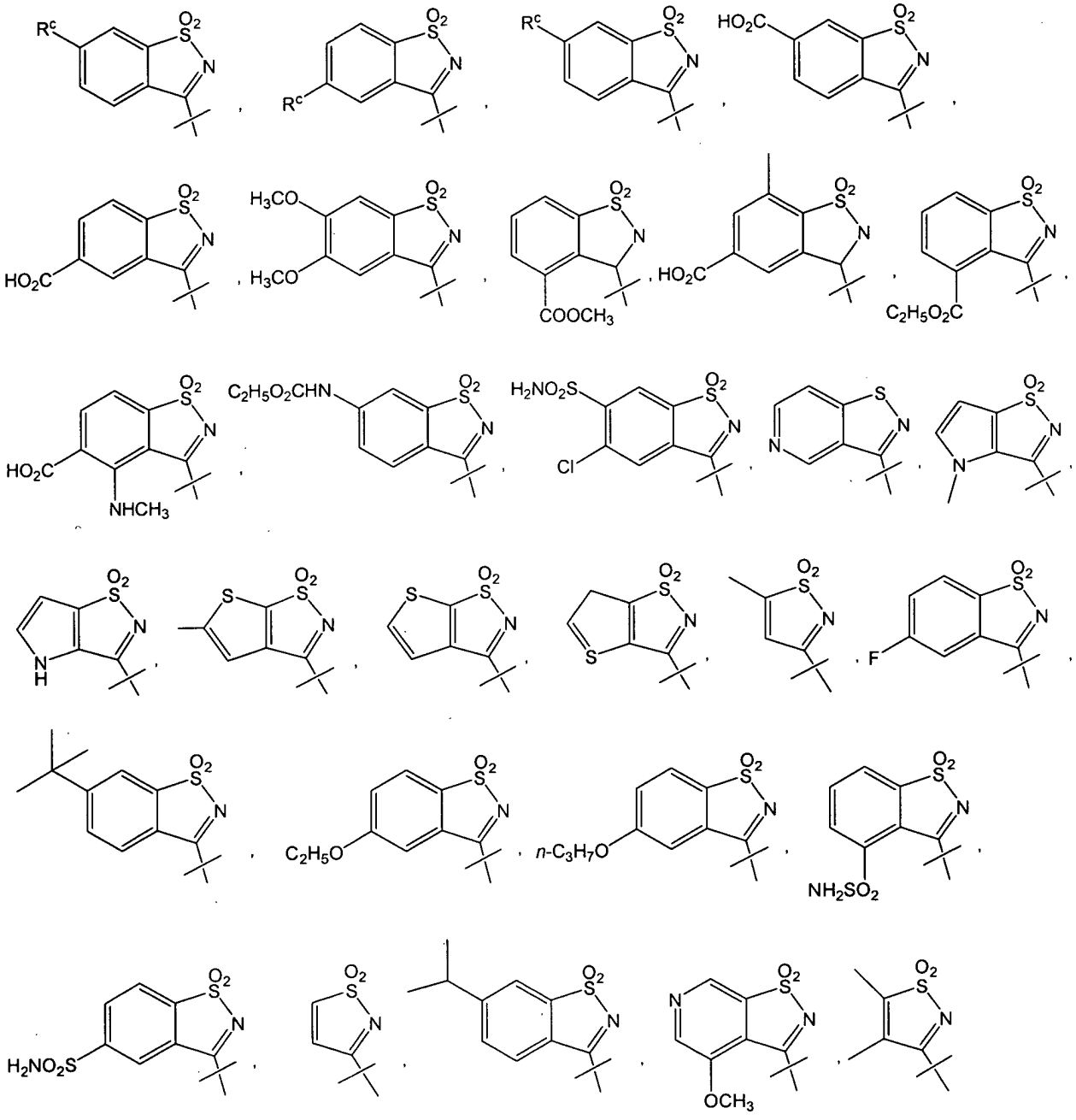
E is $-CHR^6C(O)R^{10}$ where R^6 is saturated alkyl, and R^{10} is hetero(C_{4-10})aryl optionally substituted with (C_{3-10})cycloalkyl, (C_{6-10})aryl [optionally substituted with $-NR^{28}R^{28a}$, $-OR^{29}$, or halo substituted (C_{1-4}) saturated alkyl], hetero(C_{5-10})aryl, (C_{1-6}) saturated alkyl, halo-substituted (C_{1-4}) saturated alkyl, or $-X^8OR^{29}$ where X^8 is (C_{1-6}) saturated alkylene, R^{28} and R^{28a}

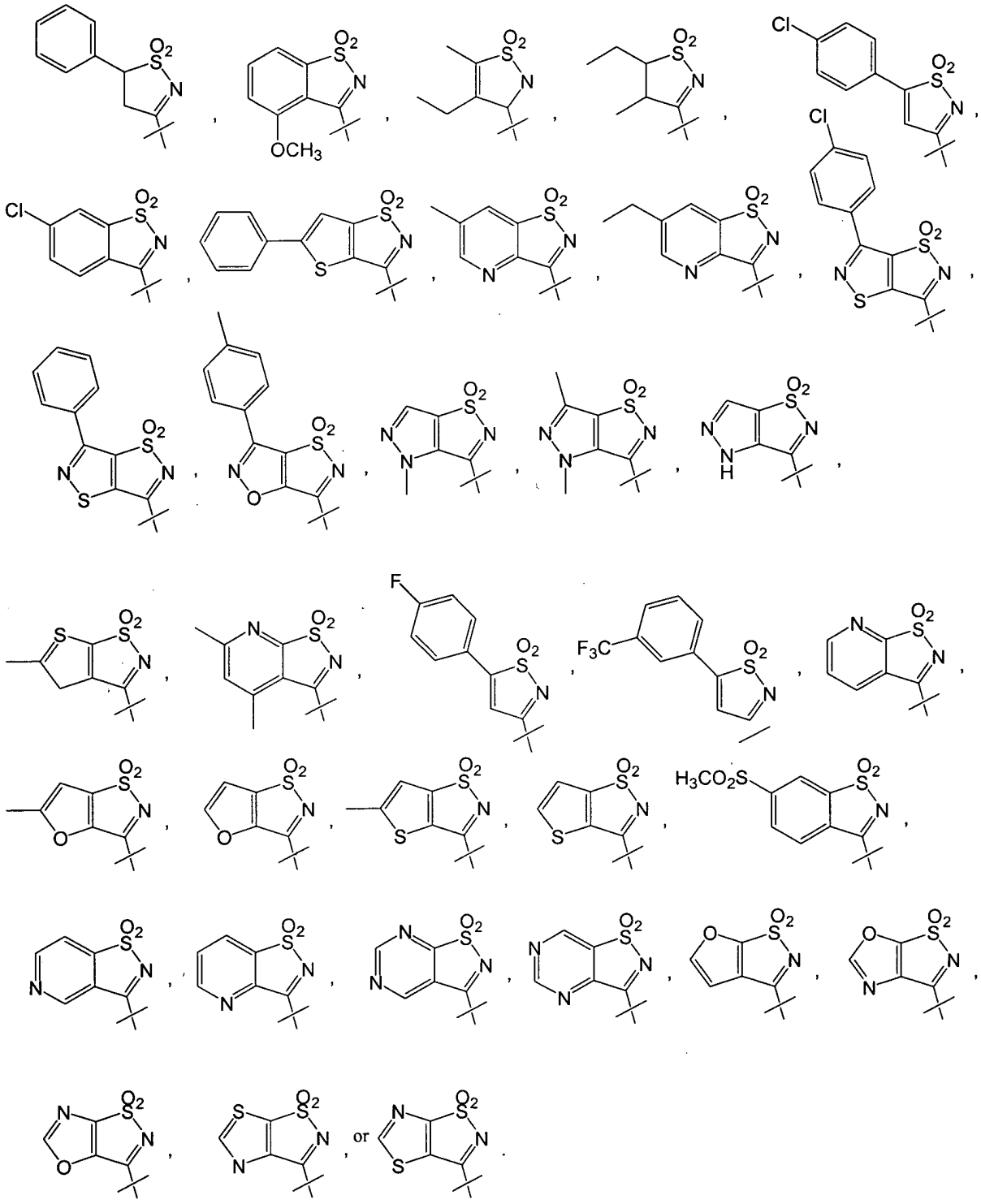
are independently hydrogen or (C_{1-6}) saturated alkyl, R^{29} is hydrogen, (C_{1-6}) saturated alkyl, or halo-substituted (C_{1-6}) saturated alkyl;

R^1 is $-CH_2X^9$ wherein X^9 is selected from $-X^{10}SR^{33}$, $-X^{10}C(O)NR^{33}R^{33a}$, $X^{10}S(O)_2R^{34}$, $-X^{10}COR^{34}$, $-X^{10}OR^{33}$, $-R^{35}$, $-X^{10}SR^{35}$, $-X^{10}S(O)_2R^{35}$, $-X^{10}C(O)R^{35,}$ or $X^{10}C(O)NR^{33}R^{35}$ wherein X^{10} is a bond or (C_{1-6})alkylene; R^{33} and ^{R33a} at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; R^{34} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl; and R^{35} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-10})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-10})bicycloaryl(C_{0-6})-alkyl wherein within R^1 any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C_{1-6}) saturated alkyl, benzyl, cyano, halo, halo-substituted(C_{1-4}) saturated alkyl, $-OR^{36}$, or $-R^{38}$ where R^{36} is (C_{1-6}) saturated alkyl or halo-substituted(C_{1-6}) saturated alkyl and R^{38} is (C_{6-10})aryl and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo; and

R^3 and R^4 together with the atoms to which they are attached form a group selected from:




R^c
HO2C
H3CO
COOCH3
C2H5O2C
C2H5O2CHN
H2NO2S
NHCH3
Cl
F
C2H5O
n-C3H7O
NH2SO2
OCH3



where R^c is amino, methylsulfonylamino, ethylsulfonylamino, methylamino, dimethylamino, acetylamino, methoxy, ethoxy, methylaminocarbonyl, aminocarbonyl, diethylaminocarbonyl, dimethylaminocarbonyl, methylaminocarbonyl, ureido, or ethoxycarbonylamino.

16. (Original) The compound of Claim 15 wherein R^I is 2,2-dichloroethyl, 2,2,2-trichloroethyl, isopropylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, *tert*-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonyl-methyl, pyridin-4-yl-methanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethane-sulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-dichloropropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothien-2-ylmethyl, pyridin-4-ylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl.

17. (Original) The compound of Claim 16 wherein R^6 ethyl and R^{10} is benzoxazol-2-yl, oxazolo[4,5-b]pyridin-2-yl, 2-pyridin-3-yl-[1,3,4]-oxadiazol-5-yl, 2-pyridin-4-yl-[1,3,4]-oxadiazol-5-yl, 2-ethyl-[1,3,4]-oxadiazol-5-yl, 2-isopropyl-[1,3,4]-oxadiazol-5-yl, 2-tert-butyl-[1,3,4]-oxadiazol-5-yl, 2-phenyl-[1,3,4]-oxadiazol-5-yl, 2-methoxymethyl-[1,3,4]-oxadiazol-5-yl, 2-furan-2-yl-[1,3,4]-oxadiazol-5-yl, 2-thien-2-yl-[1,3,4]-oxadiazol-5-yl, 2-(4-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-dimethylaminophenyl)-[1,3,4]-oxadiazol-5-yl, pyradizin-3-yl, pyrimidin-2-yl, 3-phenyl-[1,2,4]-oxadiazol-5-yl, 3-ethyl-[1,2,4]-oxadiazol-5-yl, 3-cyclopropyl-[1,2,4]-oxadiazol-5-yl, 3-thien-3-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-4-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-2-yl-[1,2,4]-oxadiazol-5-yl, 5-ethyl-[1,2,4]-oxadiazol-3-yl, 5-phenyl-[1,2,4]-oxadiazol-3-

yl, 5-thien-3-yl-[1,2,4]-oxadiazol-3-yl, 5-trifluoromethyl-[1,2,4]-oxadiazol-3-yl, 5-pyridin-4-yl-[1,2,4]-oxadiazol-3-yl, or 5-phenyloxazol-2-yl.

18. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

19. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 11, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

20. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 12, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

21. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 13, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

22. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 14, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

23. (Original) A method for treating a disease in an animal mediated by cysteine proteases, in particular cathepsin K, S, or F, which method comprises administering to the animal a pharmaceutical composition pharmaceutical composition comprising a therapeutically effective

amount of a compound of Claim 1, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

24. (Original) A method for treating a disease in an animal mediated by Cathepsin S which method comprises administering to the animal a pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 11, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

25. (Original) A method for treating a disease in an animal mediated by Cathepsin S which method comprises administering to the animal a pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 12, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

26. (Original) The method of Claim 23 wherein the disease is psoriasis.

27. (Original) The method of Claim 25 wherein the disease is psoriasis.